Substitute for PTO-1390 (Rev. 07-2005) "Transmittal Letter to the United States Designated/Elected Office(DO/EO/US)Concerning a Submission Under 35 U.S.C. 371" Approved for use through 3/31/2007. OMB 0651-0021

| Approved for use through 3/31/2007.  | JMIB 0031-0021   |   |  |  |  |  |  |
|--|--|---|--|--|--|--|--|
| U. S. PATENT AND TRADEMARK OFFICE U.S. DEPARTMENT OF COMMERCE  |  | ATTORNEY'S DOCKET NUMBER                        |  |  |  |  |  |
|  |  | Т1639ҮР   |  |  |  |  |  |
| TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)   |  | U.S. APPLICATION NO. (If known, see 37 CFR 1.5) |  |  |  |  |  |
| CONCERNING A FILI  | NG UNDER 35 U.S.C. 371   | 10/578855                                       |  |  |  |  |  |
| INTERNATIONAL APPLICATION NO   |  | PRIORITY DATE CLAIMED                           |  |  |  |  |  |
| PCT/GB2004/004816  | November 12, 2004  | November 14, 2003                               |  |  |  |  |  |
| TITLE OF INVENTION BICYCLIC PYRIMIDIN-4(3H)-ON FUNCTION OF THE VANILLOID- APPLICANT(S) FOR DO/EO/US  |  | ATIVES THEREOF WHICH MODULATE THE               |  |  |  |  |  |
| Tracy Bayless, Gregory John Holling  | gworth, Rebecca Elizabeth Jarvis, A. Bria  | an Jones, Timothy Jason Sparey                  |  |  |  |  |  |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:                                      |  |   |  |  |  |  |  |
| 1. X This is a FIRST submission  | n of items concerning a filing under 35 U  | U.S.C. 371.                                     |  |  |  |  |  |
| 2. This is a <b>SECOND</b> or <b>SUI</b>   | This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.      |   |  |  |  |  |  |
| 3. This is an express request to begin national examination procedures [35 U.S.C. 371(f)]. The submission must include items (5), (6), (9) and (21) indicated below. |  |   |  |  |  |  |  |
| 4. X The US has been elected (   | PCT Article 31).   |   |  |  |  |  |  |
| 5. X A copy of the International   | Application as filed [35 U.S.C. 371(c)(2   | 2)]   |  |  |  |  |  |
| a. is attached hereto (r   |  |   |  |  |  |  |  |
| b. 🔀 has been communic   | b. X has been communicated by the International Bureau.  |   |  |  |  |  |  |
| c. is not required, as the   | c. is not required, as the application was filed in the United States Receiving Office (RO/US).                |   |  |  |  |  |  |
| 6. An English language translation of the International Application as filed [35 U.S.C. 371(c)(2)].  |  |   |  |  |  |  |  |
| a. is attached hereto  |  |   |  |  |  |  |  |
|  | b. has been previously submitted under 35 U.S.C. 154(d)(4).  |   |  |  |  |  |  |
|  | [55 6:5:6:57,1(6)(5)].   |   |  |  |  |  |  |
|  | b. have been communicated by the International Bureau.   |   |  |  |  |  |  |
| phones .   |  |   |  |  |  |  |  |
| _  |  |   |  |  |  |  |  |
| 8. An English language transl  | An English language translation of the amendments to the claims under PCT Article 19 [35 U.S.C. 371(c)(3)].    |   |  |  |  |  |  |
| 9. X An oath or declaration of the   | An oath or declaration of the inventor(s) [35 U.S.C. 371(c)(4)].   |   |  |  |  |  |  |
| Article 36 [35 U.S.C. 371(   | c)(5)].  | Preliminary Examination Report under PCT        |  |  |  |  |  |
| Items 11 to 20 below concern other   | er document(s) or information include  |   |  |  |  |  |  |
|  | Statement under 37 CFR 1.97 and 1.98.  |   |  |  |  |  |  |
| 12. An assignment document for is included.  |  |   |  |  |  |  |  |
| 13. A preliminary amendment.   |  |   |  |  |  |  |  |
| 14. An Application Data Sheet  | An Application Data Sheet under 37 CFR 1.76.   |   |  |  |  |  |  |
| 15. A substitute specification.  |  |   |  |  |  |  |  |
| 16. A power of attorney and/or   |  |   |  |  |  |  |  |
| 17. A computer-readable form   | A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821 - 1.825. |   |  |  |  |  |  |
| 8. A second copy of the published International Application under 35 U.S.C.154(d)(4).  |  |   |  |  |  |  |  |
| 19. A second copy of the Engli   | A second copy of the English language translation of the international application under 35 U.S.C.154(d)(4).   |   |  |  |  |  |  |
| 20. Other items or information:  |  |   |  |  |  |  |  |
|  |  |   |  |  |  |  |  |
|  |  |   |  |  |  |  |  |
|  |  |   |  |  |  |  |  |

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| Approved for use t   | hrough 3/31/2007 OMB ( | 651-0021    |   |                  |                        |              |
|--|------------------------|-------------|---|------------------|------------------------|--------------|
| U.S. APPLICATION NO. (If la  |                        | INTERN      | ATTONAL APPLICATION NO.                             |                  | ATTORNEY'S DOC         | KET NUMBER   |
| 10/5   | 78855                  | PCT/GI      | 32004/004816  |                  | T1639YP                |              |
| The following fees are   | e submitted:           |             |   |                  | CALCULATIONS           | PTO USE ONLY |
| . (2.3)  |                        |             | ·····   | \$300            | \$300.00               |              |
| 22. Examination fee (37 CFR 1.492(c))  If the written opinion prepared by ISA/US or the international preliminary examination report  prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)   |                        |             |   |                  | \$200.00               |              |
| 23. Search fee (37 CFR 1.492(b))  If the written opinion of the ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)  |                        |             |   |                  | \$400.00               |              |
|  | <del></del>            | _           |   | 21, 22 and 23=   | \$900.00               |              |
| Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.  |                        |             |   |                  |                        |              |
| Total Sheets Extr  | a Sileets I            |             | additional 50 or fraction to a whole number)        | RATE             |                        |              |
| 99 - 100 = 0   | /50 0                  |             | 0   | X \$250.00       | \$0.00                 |              |
| Surcharge of \$130.00 for further priority date [37 CFR 1.492  | •                      | laration la | ter than 30 months from the                         | earliest claimed |                        |              |
| CLAIMS   | NUMBER FILED           |             | NUMBER EXTRA  | RATE             |                        | <u> </u>     |
| Total Claims   | 11                     | - 20 =      | 0   | X \$50.00        | \$0.00                 |              |
| Independent Claims   | 2                      | - 3 =       | 0   | X \$200.00       | \$0.00                 |              |
| MULTIPLE DEPENDENT   | CLAIM(S) (if applicabl | e)          |   | + \$360.00       |                        |              |
| TOTAL OF ABOVE CALCULATIONS (SUBTOTAL) =   |                        |             |   | \$900.00         |                        |              |
| Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)].  |                        |             |   |                  |                        |              |
| TOTAL NATIONAL FEE =   |                        |             |   |                  | \$900.00               |              |
| Fee for recording the enclose accompanied by an appropriate to the second secon |                        |             | _   | +                |                        |              |
|  |                        |             | TOTAL FEES ENCLO                                    | OSED =           | \$900.00               |              |
|  |                        |             |   |                  | Amount to be refunded: |              |
|  |                        |             |   |                  | Amount to be charged:  |              |
| a. A check in th   |                        |             |   |                  |                        |              |
| b. Please charge my Deposit Account No. 13-2755 in the amount of \$900.00 to cover the above fees.  A duplicate copy of this sheet is enclosed.  |                        |             |   |                  |                        |              |
|  |                        |             | charge any additional fees 3-2755. A duplicate copy |                  |                        |              |
| NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive [37 CFR 1.137(a) or (b)] must be filed and granted to restore the International Application to pending status.  |                        |             |   |                  |                        |              |
| SEND ALL CORRES  | PONDENCE TO:           |             |   |                  |                        |              |
| Customer No. 000210  |                        |             |   |                  |                        |              |
| MERCK & CO., INC.  |                        |             |   |                  |                        |              |
| Patent Department, RY60-30 P.O. Box 2000 SIGNATURE   |                        |             |   |                  |                        | <del></del>  |
| 126 East Lincoln Aver  |                        |             | 51  | GNATURE          |                        |              |
| Rahway, New Jersey   | 07065-0970             |             |   | avid A. Rubin    |                        |              |
| DATE: May 11, 2006   | 5                      |             | N   | AME              |                        |              |
| PHONE #: (732) 594-2675 40.314  REGISTRATION 1   |                        |             | IMRER   |                  |                        |              |
| i .  |                        |             | N.  | POTRICIALION     | U1-11-01-1             |              |

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## IAP12 Rec'd PCT/PTO 11 MAY 2006

## Page 1A of TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

| Attorney Docket No.:       | T1639YP  |
|----------------------------|--|
| International Appln No.:   | PCT/GB2004/004816  |
| International Filing Date: | 12 November 2004   |
| Priority Date:             | 14 November 2003   |
| Title:                     | BICYCLIC PYRIMIDIN-4(3H)-ONES AND ANALOGUES<br>AND DERIVATIVES THEREOF WHICH MODULATE<br>THE FUNCTION OF THE VANILLOID-1 RECEPTOR<br>(VR1) |
| Inventors:                 | Tracy Bayless, Gregory John Hollingworth,<br>Rebecca Elizabeth Jarvis, A. Brian Jones,<br>Timothy Jason Sparey                             |

EXPRESS MAIL CERTIFICATE

DATE OF DEPOSIT May 11, 2006

EXPRESS MAIL NO. EV 660605399 US

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS EXPRESS MAIL "POST OFFICE TO ADDRESSEE" ON THE ABOVE DATE IN AN ENVELOPE ADDRESSED TO COMMISSIONER FOR PATENTS P.O. BOX 1450, ALEXANDRIA, VIRGINIA 22313-1450.

MAILED BY MAILED BY DATE